

## **REMARKS**

After entry of the amendment, Claims 1, 5-7, 31-52 remain pending in the application. Claim 1 has been amended. Claims 7, 31-34 and 51-52 have been withdrawn.

### **CLAIM REJECTIONS – 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph**

The Examiner has rejected claim 1 under 35 U.S.C. § 112, second paragraph, as indefinite in the recitation of “B7/CD28 interactions.” Claim 1 has been amended to read “interactions between B7 and CD28.”

### **CLAIM REJECTIONS – 35 U.S.C. § 112, 1<sup>st</sup> Paragraph**

The Examiner has rejected claim 1 under 35 U.S.C. § 112, first paragraph, based on the addition of new matter. As the Examiner suggests, claim 1 has been amended to read “by blocking the interactions between B7 and CD28”; support can be found for “blocking,” for example, on page 3 and “between,” for example, on page 2. Applicants reserve the right to pursue canceled subject matter in a divisional or continuation application.

The Examiner has rejected claim 1 under 35 U.S.C. § 112, first paragraph, based on the broad scope of the previously pending claims. As stated by the Examiner, the specification is enabled for “a biological reagent comprising porcine CTLA-4 that inhibits rejection of a porcine xenotransplanted organ”. Accordingly, the claims have been amended to read “A biological reagent comprising a porcine CTLA-4 that inhibits T-cell mediated rejection of a xenotransplanted porcine organ.....”. Applicants reserve the right to pursue canceled subject matter in a divisional or continuation application.

### **CLAIM REJECTIONS – 35 U.S.C. § 102(e)**

The Examiner has rejected claims 1, 5, 6, 35-38 and 41-46 under 35 U.S.C. § 102(e) as being anticipated by Larsen et al (US Patent No. 5,916,560).

The present invention is based on the discovery of the porcine CTLA4 protein and gene sequence and its use to inhibit T-cell mediated rejection of a xenotransplanted porcine organ by blocking the interaction between B7 and CD28 to prevent the activation of xenoreactive T-cells

in the recipient. Prior to the present invention, as evident by the Larsen patent, one skilled in the art attempted to overcome this type of T-cell mediated rejection by administering to the xenotransplant recipient CTLA-4 of the recipient species (i.e. human CTLA-4 to a human recipient). In contrast, the present invention teaches the administration of CTLA-4 of the donor species to the xenotransplant recipient. The inventors discovered that although CTLA-4 molecules of recipient species, such as human CTLA-4, are able to bind both recipient and donor B7, which results in an overall immunospression of the recipient, porcine CTLA-4 preferentially binds to porcine B7 found in the xenotransplanted organ and thus results in a xenograft-specific immunosuppression in the recipient (see, for example, page 3 of the specification).

Specifically, the Larsen patent teaches systemic immunosuppression using endogenous molecules from the recipient (i.e. human) to inhibit the rejection of transplanted tissues. The Larsen patent teaches methods comprising “an endogenous molecule (e.g., antigen) on a cell selected from the group consisting of gp39 and CD40 from binding its endogenous ligand and preventing an endogenous molecule on a cell selected from the group consisting of CTLA4, CD28, and B7 from binding its endogenous ligand (emphasis added).” (Citing the Larsen patent Col. 2, lines 61-67, and Col. 3, line 1). In contrast, claim 1 has been amended to recite “A biological reagent comprising porcine CTLA-4 that inhibits T-cell mediated rejection of a xenotransplanted porcine organ by blocking the delivery of co-stimulatory signal 2 in order to prevent the activation of xenoreactive T-cells in a recipient by blocking the interactions between B7 and CD28.” Further, the present invention provides for the first time the protein sequence of porcine CTLA-4 (claims 1, 5 and 6); Larsen does not provide the sequence of porcine CTLA-4. Thus, Applicants have amended the claims to require that the CTLA-4 is porcine CTLA-4 as requested by the Examiner, thus, Larsen does not anticipate the claimed invention.

#### **Claim Rejections – 35 U.S.C. § 103(a)**

The Examiner has rejected Claims 5, 35, 39, 41, 43, and 47 under 35 U.S.C. § 103(a) as obvious over the Larsen patent in view of U.S. Patent No. 6,165,476 to Strom et al. (hereinafter “the Strom patent”). Strom et al. teach that connecting members in a fusion protein by a flexible linker can increase biological activity . . . .” The Applicants respectfully submit that the Strom

patent does not make up for any of the deficiencies of the Larsen patent discussed above and thus Larsen in view of Strom does not render the present invention obvious.

Applicants thank the Examiner for indicating that claims 40, 48, and 49 are directed to allowable subject matter.

## SUMMARY

The foregoing is submitted as a full and complete response to the final Office Action mailed July 17, 2006. The Applicants and the undersigned thank Examiner Ouspenski for the consideration of these remarks.

If the Examiner believes that any issues can be resolved by telephone conference, or that any formalities exist that can be corrected by an Examiner's amendment, please contact the undersigned at (404) 572-3567.

The Commissioner is authorized to charge any underpayment of fees to Deposit Account No. 11-0980.

Date: October 17, 2006

Respectfully submitted,

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